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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
0618.054.0002

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on _____

Signature _____

Typed or printed name _____

Application Number	Filed
09/809,029	March 16, 2001

First Named Inventor
Barnardo

Art Unit	Examiner
1641	Counts, G.

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

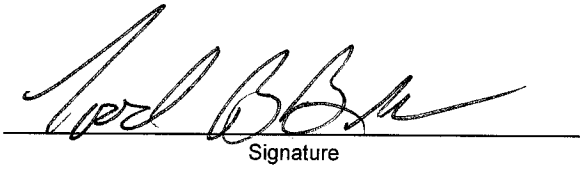
I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☐ attorney or agent of record.
Registration number 48,574.

☑ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 48,574


Signature

Todd B. Buck
Typed or printed name

202-478-5300
Telephone number

September 5, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Art Unit: 1641
Martin BARNARDO et al.	Examiner: Counts, G.
Appl. No.: 09/809,029	Atty. Docket: 0618.054.0002
Filed: March 16, 2001	Confirmation No.: 5589
For: **Method**	Customer No.: 57904

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This communication is a Request for a Pre-Appeal Brief Conference to formally review the rejections in the Final Office Action of March 3, 2006.

I. BASIS FOR REVIEW

1. Applicants request formal review of the rejection of claims 1-7, 9-17, 20 and 22-28 under the written description requirement of 35 U.S.C. §112, first paragraph.

2. Applicants request formal review of the rejection of claims 1-7, 9-17, 20 and 22-28 under the enablement requirement of 35 U.S.C. §112, first paragraph.Written Description

A. WRITTEN DESCRIPTION

Applicants respectfully assert that the Examiner's interpretation of the present claims is in clear error. The Final Office Action asserts that "[c]laims 1-7, 9-17, 20 and 22-28 are drawn to recombinant MHC molecule that binds only one antibody, ..." *Office Action of March 3, 2006,* page 2. The presently claimed invention, however, is drawn towards methods of detecting anti-MHC antibodies in a sample using recombinant MHC molecules, but is not directed to the recombinant MHC molecules themselves. In other words, the present claims do not claim

recombinant MHC molecules *per se*, but instead they claim methods of using these recombinant MHC molecules to detect anti-MHC antibodies.

Furthermore, in the Final Office Action, the Examiner states that the "recombinant molecule ... presents a unique epitope of a naturally occurring MHC allele ...." *Office Action of March 3, 2006*, page 2. Thus, although the claims do not recite such limitations to "unique epitopes" or "structurally undefined epitopes", the Examiner is imparting the recombinant MHC molecules with "unique" or "undefined" structures. While recombinant MHC molecules are elements of the claims, and therefore necessary for performance of the methods, there is no requirement that the recombinant MHC molecules of the methods claims present "structurally undefined epitopes." To the contrary, the claims and specification state that the recombinant MHC molecules must have a known identity and that the detected antibodies be specific for naturally occurring MHC alleles. Indeed, the specification states that "[t]hese recombinant MAC or MHC-type monomers, functioning as anti-MHC antibody antigens, have the advantage that the identity of the MHC is known." United States Pregrant Publication No. 2003/0017447 A1, ¶0017 (emphasis added). Furthermore, the specification indicates that, to detect anti-MHC antibodies, the recombinant MHC molecules should maintain "not only residues at the epitopic site, but also key skeletal residues to achieve correct folding of the MHC molecule to form the epitopic site." United States Pregrant Publication No. 2003/0017447 A1, ¶0026. Thus, the specification indicates that, contrary to the Examiner's interpretation of the claims, the recombinant MHC molecules should be produced to preserve epitopic sites, rather than to generate "undefined epitopes."

The Final Office Action relies heavily upon Federal Circuit precedent (*Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed Cir. 1997) and *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1216 (Fed. Cir. 2002)) to support its position that "the specification does not describe recombinant MHC molecules in a manner that satisfies either the Lilly or the Enzo standards." *Office Action of March 3, 2006*, page 4.

Unlike the facts behind the cited cases, the pending claims are not directed towards novel DNA or proteins, or methods of using novel DNA or proteins. In *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003), the claims at issue were directed to types of cells

that could be used to produce human EPO, and the court stated that "[the] Eli Lilly [decision] ... [is] inapposite to this case because the claim terms at issue here are not new or unknown biological materials that ordinarily skilled artisans would easily miscomprehend." *Amgen v. Hoechst* at 1332. The court then stated that the challengers to the Amgen-owned patent at issue "can only challenge the adequacy of the disclosure of the ... host cell – not the human DNA itself." *Id.* Similar to the facts in *Amgen v. Hoechst,* the claims here are not directed towards DNA or proteins themselves, and the claim terms here do not utilize "new or unknown biological materials that the ordinarily skilled artisan would easily miscomprehend." Rather, the claims of the pending application are directed towards methods of detecting anti-MHC antibodies using recombinant MHC molecules. The sufficiency of the disclosure in supporting the currently pending claims, therefore, must be analyzed in light of "methods of detecting anti-MHC antibodies," rather than the MHC molecules themselves.

Even more relevant to the presently claimed invention, the Federal Circuit, in overturning a decision by the Board of Patent Appeals and Interferences ("the Board"), recently clarified the written description requirement in the context of claims that utilize known biological materials in *Capon et al. v. Eshhar et al. v. Dudas,* 418 F.3d 1349 (Fed. Cir., 2005). Specifically, *Capon* clarifies the written description requirement as delineated by *Eli Lilly* and *Enzo,* among others.

In *Capon,* the claims involved in the interference were directed to a chimeric gene, which "combines segments of DNA in a way that does not occur in nature." *Capon* at 1351. The DNA components of the chimeric genes were "*known* antigen-binding-domain producing DNA and *known* lymphocyte-receptor-protein producing DNA." *Capon* at 1351 (emphasis added). The Board, however, held that "neither party's specification provides the requisite description of the full scope of the chimeric DNA or encoded proteins...." *Capon* at 1354. In support of their decision, the Board cited *Eli Lilly, Enzo* and other cases as controlling precedent.

In reviewing and overturning the Board's decision, the Federal Circuit held that "[t]he Board erred in refusing to consider the state of scientific knowledge...." *Capon* at 1357. Furthermore, the Federal Circuit stated that the Board's reliance on *Eli Lilly, Enzo* and the other "written description cases" for the case at bar was incorrect and explained that "[n]one of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e., Regents v.*

Lilly, Fiers v. Revel, Amgen [*v. Chugai*], or *Enzo Biochem*, require a re-description of what was already known." *Capon* at 1357. It is particularly noteworthy that the Federal Circuit made this assertion that nucleotide sequences need not be fully presented to satisfy the written description requirement, because the sequences of a sufficient number of sequences of the DNA chimera components were available in the published literature and methods were known and provided for linking the components of the chimera. *Capon* at 1355-1356.

Similarly, Table 4 of the present application lists multiple alleles of HLA (MHC) and their loci. The specification also points the reader to websites that depict the coding sequences of MHC molecules. In addition, methods of generating recombinant proteins were well known in the art at the time of filing. Thus, recombinant MHC molecules themselves were part of "the state of scientific knowledge" at the time of filing the application.

Accordingly, Applicants believe that, in view of properly construed claims and Federal Circuit precedent, the Examiner's rejection of claims 1-7, 9-17, 20 and 22-28 under 25 U.S.C. §112, first paragraph is in clear error. Applicants respectfully request reconsideration and withdrawal of the written description rejection.

B. ENABLEMENT

Applicants assert that the Examiner's rejection of claims 1-7, 9-17, 20 and 22-28 is in clear error. The Final Office Action states that "the specification provides no information as to structures common to … any and all recombinant MHC molecules based on structure/function correlation." *Office Action of March 3, 2006,* page 7. Further, the Office Action relies on paragraph 0026 of the currently pending published application as support for its allegations that the specification fails to enable the claimed invention.

It should be reiterated that the claims do not recite functionally equivalent derivatives or fragments of MHC molecules. The Office Action's reliance on selected passages from paragraph 0026 is therefore misplaced and taken out of context, because the cited passage in the Office Action describes "functionally equivalent variants, derivatives or fragments" of MHC molecules, which are not elements of the claim.

Thus, while the specification contemplates and describes functionally equivalent MHC molecules, the present claims do not recite such limitations. Applicants assert that the

specification fully enables the scope of recombinant MHC molecules as the claims currently read.

When the proper breadth of claims is taken into account, Applicants assert that the specification provides adequate guidance to make and use the full scope of the claimed invention, in light of the state of the art at the time of filing the application. The application contains at least 4 working examples of recombinant MHC molecules that can be used to detect anti-MHC antibodies. These working examples of at least 4 recombinant MHC molecules, however, should not limit the scope of the claims solely to constructs comprising these 4 recombinant MHC molecules. Instead, Applicants assert that, given the state of the art at the time of filing, one of skill in the art could use the teachings of the present specification to prepare additional recombinant MHC molecules. The specification is replete with listings of other HLA alleles, *e.g.*, Table 4, that could be used to generate recombinant MHC molecules. In addition, the specification directs the reader to various references and web sites that disclose nucleic acid sequences for MHC alleles.

When viewed in the context of proper claim scope and the state of the art at the time of filing, Applicants assert that the application provides ample guidance to one of skill in the art to generate recombinant MHC molecules for their use in the claimed methods of detecting anti-MHC antibodies. Applicants respectfully request reconsideration and withdrawal of the enablement rejection.

Respectfully submitted,

Date September 5, 2006

By /Todd B.Buck/

Castellano Malm Ferrario & Buck PLLC
Customer Number: **57904**
Telephone: (202) 478-5300
Facsimile: (202) 318-1288

Todd B. Buck
Registration No. 48,574